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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Elzbieta Chlopecka
Pollock Vande Sande & Amernick LLP
P O Box 19088
Washington, DC 20036-3425

EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/527,028	VERIAC ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 14-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 14-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 2/2/04 is acknowledged and has been entered. Claim 12 has been amended. Currently, claims 12 and 14-24 are pending and are under examination.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 12 and 14-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide literal support for the recitation of "the absence of nonionic detergents". Applicant points to page 6, lines 2-24 for support which generally defines anionic detergents as "cationic or ionic", and their use in dissociating protein complexes and solubilizing proteins of membranes. However, such description does not provide specific teaching or disclosure for the

recitation of a negative limitation in the claims excluding nonionic detergents. Page 6, lines 10-24 only provide that the detergent is advantageously chosen from "primary amines ... of fatty amines, quaternary ammonium salts and trimethylethylammonium bromide, the amides of substituted diamines ..., and the amides of cyclised diethylenetriamine" but still fails to provide literal support for the recitation of the negative limitation. Specific guidance for the exclusion of nonionic detergents is not taught, the recitation of the negative limitation is not supported in the instant specification, nor does it flow from the specification. Additionally, none of the originally filed claims recited the limitation in question. Recitation of a negative claim limitation lacking literal support in the specification or originally filed claims constitutes new matter. See In re ANDERSON, 176 USPQ 331 (CCPA 1973).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 12 and 14-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sakata et al. (US 5,538,893) in view of Hamaguchi et al. (US 5,389,549) for reason of record and as follows.

Sakata et al. disclose a single reagent for analyzing and classifying leucocytes including basophil, which is capable of determining cell size and morphological features of all leucocytes (see Abstract and column 6, lines 60-64). Specifically, the single reagent comprises a buffer for adjusting the pH to 2.5 - 4.0, a cationic detergent (surfactant), and also an inorganic salt. The cationic detergent includes quaternary ammonium salts for complete lysis of erythrocytes and baring the nuclei of granulocytes other than basophil (see column 4, lines 21-59). The cationic detergent is preferred at a concentration of 1 g/l to 10 g/l (see column 4, lines 53-64). The reagent buffer used includes citric acid and tartaric acid in addition to alkali metal hydroxides such as sodium hydroxide and potassium hydroxide, for adjusting pH to a desired pH of 2.0 - 5.0 (see column 5, lines 25-40). The inorganic salts include alkali metal salts such as sodium chloride and potassium chloride (see column 6, lines 1-6). According to Sakata et al., the surfactants, the buffer, and the salts are prepared and mixed at desired ratios (see column 5, lines 44-63). Sakata et al. disclose that at appropriate concentrations, cell lysing is exhibited and lymphocytes and monocytes, immature granulocytes and

basophils which include a large percentage of basophilic granules are hardly shrunk allowing differentiation in sizes of leucocytes (see column 7, lines 36-47).

In addition, Sakata et al. specifically teach an embodiment excluding or in the absence of nonionic detergents in column 7, lines 54-63 and Table 1. In this section, Sakata et al. teach that when only a cationic surfactant is used at an appropriate concentration, lymphocytes, monocytes, and immature granulocytes are hardly shrunk or difficult to shrink; granulocytes other than basophils retain part of their cytoplasm and their nuclei are not completely bared; and mononuclear cells and granulocytes other than basophils cannot be classified. In other words, Sakata et al. teach that when only a cationic surfactant is used as an appropriate concentration, only basophils can be classified; thus providing a determination of basophilic polymorphonuclear leucocytes, as recited in the claimed invention.

Sakata et al. differ from the instant invention in failing to disclose the single reagent as having a pH of 2.4 and further comprising a nitrogenous compound.

Hamaguchi et al. disclose a hematologic reagent for counting and classifying leucocytes including basophil and lysing erythrocytes. Specifically, the reagent comprises a blood diluent including a phosphate buffer which maintains the pH at 1.5 - 5.0, sodium chloride, a nonionic detergent; and a nitrogenous compound for use in reducing the size of monocytes in leucocytes. Hamaguchi et al. disclose that nitrogenous compounds are solubilizing agents which include thiourea or 1,3-dimethylurea. Specifically, Hamaguchi et al. disclose that when incorporated into a reagent, the solubilizing agent selectively promotes the action of the lysing reagent into

monocytes. Such selective action of solubilizing agents to monocytes is also effective with other reagents used in leucocyte classification. Hamaguchi et al. further disclose that the reagent comprising a buffer having potassium phthalate, hydrochloric acid, nitric acid, and a lysing agent at an acidic pH of 3.0, is enabled for basophil measurement.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the solubilizing agent / nitrogenous compound as taught by Hamaguchi into the single reagent as taught by Sakata because Hamaguchi specifically suggested conventional applicability of nitrogenous compounds with hematologic reagents used in leucocyte classification such as the reagent taught by Sakata.

In as far as the recitation of intended use, i.e. single reagent ... for use in measurement of hemoglobin", the claimed single reagent "comprising a buffer, at least one cationic detergent, and nitrogenous compound", must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In this case, the combination of Sakata with Hamaguchi which suggests a "single reagent ... comprising a buffer, at least one cationic detergent, and nitrogenous compound", renders obvious the claimed invention.

Sakata et al. and Hamaguchi et al. differ from the instant invention in failing to disclose the specific concentration parameters of elements recited in claims 23 and 24.

It is, however, maintained that the concentration parameters such as detergent [0.2-20 g/l] and nitrogenous compound [0.1-10 g/l] recited in claim 23 and potassium chloride [5-15 g/l], 1,3- dimethyl-2- thiourea [0.5-5 g/l], dodecyltrimethylammonium chloride [0.5-5 g/l], and potassium hydrogen phosphate / HCl [1.0-10 g/l] which are recited in claim 24, are all result effective variables which the prior art references have shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 23 and 24 are for any particular purpose or solve any stated problem and the prior art teaches that the different reagent elements and parameters often vary according to the reagent system used or sample being analyzed and parameters appear to work equally as well; absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable

ranges of the methods disclosed by the Sakata and Hamaguchi by normal optimization procedures known in the leucocyte differentiation art.

Response to Arguments

4. Applicant's arguments filed 2/2/04 have been fully considered but they are not persuasive.

A) Applicant argues that the cited references, Sakata et al. and Hamaguchi et al., fail to teach the new limitation incorporated into claim 1, "the absence of nonionic detergents". Applicant specifically contends that Sakata et al. teach away from the claimed invention in failing to teach exclusion of nonionic detergents.

Contrary to Applicant's argument, Sakata et al. does teach an embodiment excluding the use of anionic detergents in column 7, lines 54-63 wherein only a cationic surfactant is used at an appropriate concentration, resulting in difficulty to shrink lymphocytes, monocytes, and immature granulocytes; retention of cytoplasm of granulocytes other than basophils, thus having nuclei that are not completely bared; so that none of the leucocytes, i.e. mononuclear cells and granulocytes, other than basophils are classified. In other words, Sakata et al. teach that when only a cationic surfactant is used as an appropriate concentration, only basophils can be classified; thus providing a determination of basophilic polymorphonuclear leucocytes, as recited in the claimed invention.

B) Applicant argues that Sakata et al. teaches away from the present invention in failing to teach a pH of 2.4 as recited in claim 14.

In response, the rejection is based on the combination of the teaching of Sakata et al. with Hamaguchi et al. supra. While Sakata et al. differs in failing to disclose a reagent having a pH of 2.4, Hamaguchi et al. is relied upon for the teaching of a single reagent having a pH of 1.5 to 5.0; thus, encompassing a pH of 2.4, as recited in the claimed invention.

5. No claims are allowed.

6. Applicant's amendment necessitated the new ground of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
March 25, 2004

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641